

Amendment to the Claims

1-80. (Canceled)

81. (New) A polypeptide capable of modulating an immune response against a molecule, the polypeptide comprising:

- (a) a first portion being an Fve polypeptide (SEQ ID NO: 6), a fragment thereof comprising at least 20 amino acids or a polypeptide having at least 70% sequence identity thereto, which polypeptide or fragment comprises immunomodulatory activity; and
- (b) a second portion being a molecule against which the modulation of the immune response is desired.

82. (New) A polypeptide according to Claim 81, in which the second portion comprises an allergen or a fragment thereof.

83. (New) A polypeptide according to Claim 82, in which the allergen comprises an allergen from a mite, preferably from Family *Glycyphagidae* or Family *Pyroglyphidae*, preferably a group 1 allergen (Der p 1, Der f 1, Blo t 1, Eur m1, Lep d 1), a group 2 allergen (Der p 2, Der f 2, Blo t 2, Eur m 2, Lep d 2), a group 5 allergen (Blo t 5, Der p 5, Der f 5, Eur m 5, Lep d 5) a group 15 allergen (Der p 15, Der f 15, Blo t 15, Eur m 15, Lep d 15).

84. (New) A polypeptide according to Claim 82 or 83, which polypeptide is selected from the group consisting of: Blo t 5-Fve (SEQ ID NO: 38), Blo t 5-FveR27A (SEQ ID NO: 40), Blo t 5-FveT29A (SEQ ID NO: 42), Der p 2-Fve, Der p 2-FveR27A (SEQ ID NO: 44), Der p 2-FveT29A (SEQ ID NO: 46), GST-Der p 2-FveR27A, GST-Der p 2-FveT29A, Blo t 5-Der p 2-FveR27A (SEQ ID NO: 48) and Blo t 5-Der p 2-FveT29A.

85. (New) A polypeptide according to Claim 82, in which the allergen is selected from the group consisting of: tree pollen allergen, Bet v 1 and Bet v 2 from birch tree; grass pollen allergen, Phl p 1 and Phl p 2 from timothy grass; weed pollen allergen, antigen E from

ragweed; major feline antigen, Fel d; major fungal allergen, Asp f1, Asp f2, and Asp f3 from *Aspergillus fumigatus*.

86. (New) A polypeptide according to Claim 81, in which the second portion comprises a viral antigen or a fragment thereof, the viral antigen preferably being selected from the group consisting of: E6 and E7 from HPV; core Ag and E2 from HCV; core and surface antigens from HBV; LMP-1, LMP-2, EBNA-2, EBNA-3 from EBV; Tax from HTLV-1 and antigens from Adenovirus, Parainfluenza 3 virus, Human Immunodeficiency Virus (HIV-1, HIV-2), Herpes simplex virus (HSV), Respiratory syncytial virus (RSV), Influenza A virus, Flu A, coronavirus and flavivirus.

87. (New) A polypeptide according to Claim 86 which comprises HPV E7-FveT29A (SEQ ID NO: 49) or HCV Core23-FveT29A (SEQ ID NO: 51).

88. (New) A polypeptide according to Claim 81, in which the second portion comprises a tumour-associated antigen or a fragment thereof, the tumour-associated antigen preferably being selected from the group consisting of: MAGE-1, MAGE-2, MAGE-3, preferably a sequence, BAGE, GAGE, PRAME, SSX-2, Tyrosinase, MART-1, NY-ESO-1, gp100, TRP-1, TRP-2, A2 melanotope, BCR/ABL, Proteinase-3/Myeloblastin, HER2/neu, CEA, P1A, HK2, PAPA, PSA, PSCA, PSMA, pg75, MUM-1, MUC-1, BTA, GnT-V, β -catenin, CDK4, and P15.

89. (New) A polypeptide according to Claim 88 which comprises MAGE3-FveT29A (SEQ ID NO: 53), MART1-FveT29A (SEQ ID NO: 55) or CEA-FveT29A (SEQ ID NO: 57).

90. (New) A polypeptide according to any preceding claim, in which the first portion comprises between 2 to 20 residues of amino acid sequence flanking the glycine residue corresponding to position 28 of Fve.

91. (New) A polypeptide according to any preceding claim, in which the first portion comprises the sequence RGT or the sequence RGD.

92. (New) A polypeptide according to Claim 91 comprising an sequence selected from the group consisting of: Fve R27A (SEQ ID NO: 32), Fve T29A (SEQ ID NO: 36), GST-Fve R27A and GST-Fve T29A.

93. (New) A nucleic acid encoding a polypeptide according to any preceding claim.

94. (New) A nucleic acid according to Claim 93, in which the nucleic acid comprises CGT GGT ACC, or a sequence which differs from the above by virtue of the degeneracy of the genetic code and which encodes a sequence RGT.

95. (New) A nucleic acid according to Claim 93 or 94, which comprises (a) Blo t 5-Fve (SEQ ID NO: 37), Blo t 5-FveR27A (SEQ ID NO: 39), Blo t 5-FveT29A (SEQ ID NO: 41), Der p 2-Fve, Der p 2-FveR27A (SEQ ID NO: 43), Der p 2-FveT29A (SEQ ID NO: 45), GST-Der p 2-FveR27A, GST-Der p 2-FveT29A, Blo t 5-Der p 2-FveR27A (SEQ ID NO: 47) or Blo t 5-Der p 2-FveT29A; (b) HPV E7-FveT29A (SEQ ID NO: 50) or HCV Core23-FveT29A (SEQ ID NO: 52); (c) MAGE3-FveT29A (SEQ ID NO: 54), MART1-FveT29A (SEQ ID NO: 56) or CEA-FveT29A (SEQ ID NO: 58); or (d) Fve R27A (SEQ ID NO: 31), Fve T29A (SEQ ID NO: 35), GST-Fve R27A or GST-Fve T29A.

96. (New) A vector, preferably an expression vector, comprising a nucleic acid sequence according to any of Claims 93 to 95.

97. (New) A DNA vaccine, a host cell or a transgenic non-human organism, preferably a bacterium, a yeast, a fungus, a plant or an animal, more preferably a mouse, comprising a nucleic acid according to any of Claims 93 to 95 or a vector according to Claim 96.

98. (New) A pharmaceutical composition comprising a polypeptide according to any of Claims 81 to 92, a nucleic acid according to any of Claims 93 to 95, a vector according to Claim 96, or a DNA vaccine or a host cell according to Claim 97, together with a pharmaceutically acceptable carrier or diluent.

99. (New) A polypeptide, nucleic acid, vector, DNA vaccine, host cell or a pharmaceutical composition according to any of Claims 81 to 98 for use in the treatment of a disease.

100. (New) Use of a polypeptide, nucleic acid, vector, DNA vaccine, host cell or a pharmaceutical composition according to any of Claims 81 to 98 for the preparation of a pharmaceutical composition for the treatment of a disease.

101. (New) Use of a polypeptide, nucleic acid, vector, DNA vaccine, host cell or a pharmaceutical composition according to any of Claims 81 to 98 as an immunomodulator, to enhance an immune response in a mammal, or as an adjuvant for a vaccine or in a method of treatment or prophylaxis of a disease.

102. (New) A method of treating an individual suffering from a disease or preventing the occurrence of a disease in an individual, the method comprising administering to the individual a therapeutically or prophylactically effective amount of a polypeptide, nucleic acid, vector, DNA vaccine, host cell or a pharmaceutical composition according to any of Claims 81 to 98.

103. (New) A use or method according to any of Claims 100 to 102, in which the disease comprises an atopic disease or allergy.

104. (New) A use or method according to Claim 103, in which the allergy is selected from the group consisting of: allergic asthma, a seasonal respiratory allergy, a perennial respiratory allergy, allergic rhinitis, hayfever, nonallergic rhinitis, vasomotor rhinitis, irritant

rhinitis, an allergy against grass pollen, weed pollen, tree pollen or animal danders, an allergy associated with allergic asthma and a food allergy.

105. (New) A use or method according to Claim 103 or 104, in which the allergy is to a house dust mite from Family Glyphagidae, preferably *Blomia tropicalis* or from Family Pyroglyphidae, preferably *Dermatophagoides pteronyssinus* or *Dermatophagoides farinae*, or to fungi or fungal spores, preferably *Aspergillus fumigatus*, or to tree pollen allergens, preferably from birch tree, or grass pollen allergens, preferably from timothy grass, or weed allergens, preferably ragweed.

106. (New) A use or method according to any of Claims 100 to 102, in which the disease comprises a cancer, preferably by suppressing tumour progression.

107. (New) A use or method according to Claim 106, in which the cancer comprises a T cell lymphoma, leukaemia, brain neoplasms, bladder cancer, renal cancer, hepatoma, melanoma, lung cancer, colon cancer, breast cancer or prostate cancer.

108. (New) Use of a polypeptide comprising an Fve sequence, a fragment thereof or a polypeptide having at least 70% sequence identity thereto, which polypeptide or fragment comprises immunomodulatory activity, a nucleic acid encoding such or a polypeptide according to any of Claims 81 to 92 in a method of stimulating proliferation of CD3⁺ CD8⁺ CD18⁺ bright T cells.

109. (New) Use of a polypeptide according to any of Claims 81 to 92, an Fve polypeptide, a fragment thereof or a polypeptide having at least 70% sequence identity thereto, which polypeptide or fragment comprises immunomodulatory activity, or a nucleic acid encoding any of the above, in a method of enriching natural killer (NK) T cells in a cell population, or enhancing cytolytic activity of CD16⁺ CD56⁺ natural killer (NK) T cells.

110. (New) Use of a polypeptide according to any of Claims 81 to 92, an Fve polypeptide, a fragment thereof or a polypeptide having at least 70% sequence identity thereto, which polypeptide or fragment comprises immunomodulatory activity, or a nucleic acid encoding any of the above, in a method of stimulating production of IL-10 in CD3⁺ cells.

111. (New) Use according to Claim 110, in which production of IL-4 and IL-13 are not stimulated in the CD3⁺ cells.

112. (New) A method of amplifying a sub-population of cells, the method comprising: (a) obtaining a population of cells from an individual; (b) amplifying CD3⁺ CD8⁺ and CD18⁺ bright T cells by exposing the population of cells to a polypeptide according to any of Claims 81 to 92, an Fve polypeptide, a fragment thereof or a polypeptide having at least 70% sequence identity thereto, which polypeptide or fragment comprises immunomodulatory activity, or a nucleic acid encoding any of the above.

113. (New) A method according to Claim 112, further comprising the step of: (c) isolating the CD3⁺ CD8⁺ and CD18⁺ bright T cells.

114. (New) A method of treating an individual suffering from a disease or preventing the occurrence of a disease in an individual, the method comprising amplifying a CD3⁺ CD8⁺ and CD18⁺ bright T cell by a method according to Claim 112 or 113, and administering the amplified CD3⁺ CD8⁺ and CD18⁺ bright T cell to an individual.

115. (New) A variant Fve polypeptide comprising a Fve polypeptide having a sequence set out in SEQ ID NO: 6 together with a mutation at position 27 of that sequence, or a mutation at position 29 of that sequence, or both.

116. (New) A variant Fve polypeptide according to Claim 115, in which the mutation or mutations independently comprise a substitution to a neutral residue such as glycine (G) or alanine (A).

117. (New) A variant Fve polypeptide according to Claim 115 or 116, in which a mutation at position 27 comprises R27A.

118. (New) A variant Fve polypeptide according to Claim 115, 116 or 117, in which a mutation at position 29 comprises T29A.

119. (New) A variant Fve polypeptide according to any of Claims 115 to 118, comprising mutations at both position 27 and position 29, preferably R27A and T29A.

120. (New) A variant Fve polypeptide according to any of Claims 115 to 119, comprising an sequence selected from the group consisting of: Fve R27A (SEQ ID NO: 32), Fve T29A (SEQ ID NO: 36), GST-Fve R27A, and GST-Fve T29A.

121. (New) A variant Fve polypeptide according to any of Claims 115 to 120, which has an increased activity as compared to the wild type Fve polypeptide (SEQ ID NO: 6) selected from the group consisting of: up-regulation of expression of Th1 cytokines, preferably IFN- γ and TNF- α , down-regulation of expression of Th2 cytokines, preferably IL-4 and IL-13, hemagglutination activity, cell aggregation activity, lymphocyte aggregation activity, lymphoproliferation activity, up-regulation of expression of IL-2, IFN- γ , TNF- α , but not IL-4 in CD3⁺ T cells, interaction with T and NK cells, adjuvant activity, stimulation of CD3⁺ CD16⁺ CD56⁺ natural killer (NK) T cells, and up-regulation of expression of allergen specific IgG2a antibody.

122. (New) A variant Fve polypeptide according to any of Claims 115 to 121, which has an increased solubility compared to the wild type Fve polypeptide (SEQ ID NO: 6).

123. (New) A variant Fve polypeptide which is derivable from a parent polypeptide having the sequence SEQ ID NO: 6, in which the variant Fve polypeptide comprises an amino

acid mutation at position 27, or an amino acid mutation at position 29, or both, with reference to the position numbering of SEQ ID NO: 6.

124. (New) A fragment of a variant Fve polypeptide according to any of Claims 115 to 123, which comprises at least 20 residues of amino acid sequence flanking the glycine residue at position 28 of Fve, with reference to the position numbering of SEQ ID NO: 6, which fragment has increased solubility when compared to wild type Fve (SEQ ID NO: 6).

125. (New) A nucleic acid capable of encoding a variant Fve polypeptide according to any of Claims 115 to 124.

126. (New) A nucleic acid according to Claim 125, which is selected from the group consisting of: Fve R27A (SEQ ID NO: 31), Fve T29A (SEQ ID NO: 35), GST-Fve R27A and GST-Fve T29A.

127. (New) A vector, preferably an expression vector, comprising a nucleic acid sequence according to Claim 125 or 126.

128. (New) A DNA vaccine, a host cell or a transgenic non-human organism, preferably a bacterium, a yeast, a fungus, a plant or an animal, more preferably a mouse, comprising a nucleic acid according to Claim 125 or 126 or a vector according to Claim 127.

129. (New) A pharmaceutical composition comprising a variant Fve polypeptide according to any of Claims 115 to 124, a nucleic acid according to any of Claims 125 to 126, a vector according to Claim 127, or a DNA vaccine or a host cell according to Claim 128, together with a pharmaceutically acceptable carrier or diluent.

130. (New) A polypeptide, nucleic acid, vector, DNA vaccine, host cell or a pharmaceutical composition according to any of Claims 115 to 129 for use in the treatment of a disease.

131. (New) Use of a polypeptide, nucleic acid, vector, DNA vaccine, host cell or a pharmaceutical composition according to any of Claims 115 to 129 for a purpose as set out in any of Claims 100 to 114.

132. (New) Use of an Fve polypeptide (SEQ ID NO: 6), a fragment thereof comprising at least 20 amino acids or a polypeptide having at least 70% sequence identity thereto, which polypeptide or fragment comprises immunomodulatory activity, as an adjuvant.

133. (New) A method of modulating an immune response against a molecule, the method comprising simultaneously or sequentially administering to an individual:

- (a) a first molecule being an Fve polypeptide (SEQ ID NO: 6), a fragment thereof comprising at least 20 amino acids or a polypeptide having at least 70% sequence identity thereto, which polypeptide or fragment comprises immunomodulatory activity; and
- (b) a second molecule being a molecule against which the modulation of the immune response is desired.

134. (New) An Fve polypeptide (SEQ ID NO: 6), a fragment thereof comprising at least 20 amino acids or a polypeptide having at least 70% sequence identity thereto, which polypeptide or fragment comprises immunomodulatory activity for use in a method of modulating an immune response against a molecule.

135. (New) An Fve polypeptide, fragment or polypeptide according to Claim 134 for a use as specified therein, in which the method comprises simultaneously or sequentially administering to an individual the Fve polypeptide, fragment or polypeptide and a molecule against which the modulation of the immune response is desired.

136. (New) A method according to Claim 133 or an Fve polypeptide, fragment or polypeptide according to Claim 134 or 135 for a use as specified therein, further comprising a feature as set out in any of Claims 82 to 92.

137. A method according to Claim 133 or 136 or an Fve polypeptide, fragment or polypeptide according to Claim 134 or 135 or 136 for a use as specified therein, in which the first molecule or Fve polypeptide comprises a variant Fve polypeptide or fragment as claimed in any of Claims 105 to 124.